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# **Proactive Inhibition: An Element Of Inhibitory Control In Eating Disorders**

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## Abstract

The aetiology of eating disorders (EDs) is unclear, but many hypotheses implicate alterations in behavioural control. Specifically and because of its relevance to symptomatology, there has been much interest in inhibitory control, i.e., the ability to inhibit inappropriate/ unwanted behaviours. This has been studied in relation to reactive motor inhibition (withholding a response in reaction to a signal), reward-based inhibition (e.g., temporal discounting paradigms) and to reversal learning (e.g., set shifting tasks assessing cognitive flexibility and compulsivity). However, there has been less explicit exploration of *proactive* inhibitory control, i.e., a preparatory form of inhibitory control where responses are pre-emptively suppressed to improve performance either in terms of a dynamic strategy (e.g., post-error slowing) or as a more general suppression in the context of uncertainty (e.g., when the appropriateness of a response is less certain). This review considers proactive inhibition within the context of broader conceptual considerations of inhibitory control in EDs, discusses the existing behavioural and neural evidence, and concludes that this is a construct worthy of further exploration.

## Keywords

Proactive inhibition; eating disorders; inhibitory control

## 1. Introduction

Eating disorders (EDs) are serious psychiatric disorders characterised by extreme dietary practices and pathological concerns over weight and shape (American Psychiatric Association, 2013).

However, the mechanisms underlying the development and maintenance of EDs remain unclear (Kaye et al., 2015; Wu et al., 2013b). Investigations into the aetiology of EDs have predominantly employed experimental and neurobiological approaches that explore behavioural, cognitive and affective concepts, and the way in which these all interact. These include behavioural control, reward sensitivity, cognitive flexibility and anxiety.

Altered behavioural control and experience thereof is relevant to a number of core behavioural symptoms of EDs. For example, chronic food restriction may be associated with attempts to establish control, or with a loss of control over the ability to regulate food consumption. The experience of a loss of control is part of the definition of a binge eating episode (American Psychiatric Association, 2013). Individuals may engage in food restriction or purging behaviours such as self-induced vomiting or laxative use, to compensate for potential weight gain or the effects of overeating: as such, they reflect an attempt to re-establish control over weight/eating. However, purging episodes can also be experienced as being uncontrollable, with uncontrollable binge eating and purging being an indicator for potential hospital admission (Golden et al., 2015). In addition, EDs are highly comorbid with a number of psychiatric symptoms/disorders that are characterised by altered behavioural control, including suicidal behaviour (Franko & Keel, 2006), attention deficit hyperactivity disorder (Biederman et al., 2007; Nazar et al., 2008) and obsessive compulsive disorder (Blinder et al., 2006; Kaye et al., 2004). The odds of a comorbid impulse control disorder are considerably highest for BN, which is also associated with compulsive buying, shoplifting and substance abuse (e.g., Fernández-Aranda et al., 2008; Hudson et al., 2007; Mole et al., 2015; Nazar et al., 2008). In contrast, AN is not thought to be associated with substance use

disorders (Calero - Elvira et al., 2009; Gadalla & Piran, 2007), and may even be a protective factor against substance use disorders (Brooks, 2016; Kaye et al., 2013).

On the basis of the above and other studies, spectrum models of EDs have been suggested (Brooks, 2016; Brooks et al., 2012). In these, anorexia nervosa (AN) restrictive subtype (AN-R) lies at the over-controlling (inhibitory) extreme, followed by AN binge-purge subtype (AN-BP) and bulimia nervosa (BN). Binge eating disorder (BED) is placed at the impulsive extremity (in terms of appetite control). Evidence, however, suggests patients with BN are more impulsive than patients with BED in other domains, e.g., in relation to self-harm and substance misuse (Hudson et al., 2007; Wu et al., 2013b). While it is unlikely that EDs can be described using a neurocognitive model including a single domain (inhibitory control), such a model provides a useful starting point for assessing the interactions between neurocognition and other behavioural, cognitive and biological factors that may explain certain phenomenological variations within the population. For example, such a model can generate hypotheses on how the cognitive processes underlying behavioural control interact with biological and motivational systems to influence pathological behaviours (such as chronic food restriction or binge eating).

There is much interest in behavioural and cognitive inhibitory control and how they may contribute to ED psychopathology. Behaviourally, these have been studied mainly in relation to reward-based inhibition (such as in temporal discounting paradigms), cognitive flexibility (such as in set shifting tasks), or reactive inhibition (i.e., withholding a response in the context of a stop signal, as in the stop signal task or go/no-go task). It seems likely that the relative contribution of different aspects of inhibitory control varies across EDs, in a similar way to established impulse-control disorders. For example, while reactive inhibition appears to be affected to a comparable degree in OCD, ADHD and schizophrenia, there is a smaller deficit in substance use disorders and Tourette's syndrome suggesting deficient reactive response inhibition may be less central to these latter disorders (Lipszyc & Schachar, 2010). In a similar way, different types of inhibitory control may contribute to the different EDs. For example, with respect to temporal discounting (i.e., the

capacity to delay reward or gratification), individuals with AN show a greater ability to delay gratification than healthy individuals (Steinglass et al., 2012), whereas the opposite has been reported in people with BED (Davis et al., 2010; Manwaring et al., 2011; Mole et al., 2015) and BN (Kekic et al., 2016). In contrast, poorer reactive response inhibition in the stop signal task has been reported across the eating disorders (e.g., Galimberti et al., 2012; Svaldi et al., 2014; Wu et al., 2013a), although the findings are not consistent (Bartholdy et al., 2016). Thus, while there may be more disorder-specific aspects to temporal discounting in EDs, reactive inhibition may be affected in a similar way across disorders.

## **2. Proactive inhibition**

To date, in EDs there has been less explicit exploration of proactive (preparatory) approaches, i.e., processes that pre-emptively suppress or gate motor responses or response tendencies ('braking') (Criaud et al., 2012). Individuals use proactive inhibition on a daily basis, acting more cautiously or reservedly when the required outcome is unknown. For example, individuals will drive more slowly in areas where children are likely to be playing, in case a child runs into the street. Studies of EDs have indirectly explored one framework of proactive inhibition, namely strategic proactive adjustment of behaviour to improve performance (e.g., post-error slowing). While such strategic proactive inhibition is present in a number of commonly employed neuropsychological tasks, this is a complicated manifestation of proactive inhibition that may interact with or depend on a number of additional task components, including signal detection, attention, and determination of response relevance. Proactive inhibition is more simply manifested as an automatic or general suppression of responses in the context of uncertainty or aversion (i.e., rather than as a dynamic strategy), assessed using simple reaction time paradigms involving spatially-uninformative cues. This simple manifestation of proactive inhibition is relatively underexplored in EDs. In this review, we discuss the potential relevance of proactive inhibition in relation to ED symptomatology, to the neural basis of EDs, and with reference to broader conceptual considerations of inhibitory control in EDs.

### 3. Evidence of altered proactive inhibition in eating disorders

One aspect of proactive inhibition relates to the strategic adjustment of response preparation to changing environmental demands (Aron, 2011; Verbruggen & Logan, 2009; Zandbelt et al., 2013; Zandbelt & Vink, 2010). This is reflected by slower reaction times when manipulating the overall context of the response (Aron & Verbruggen, 2008). It can be assessed by dynamically adjusting the degree of uncertainty between trials in established neuropsychological tasks that assess executive function or inhibitory control. For example, differences in response time when a response is uncertain compared to when it is a certainty can be considered an index of the cost of preparing a response (Chikazoe et al., 2009). This can be explored using a modified stop signal task that compares reaction time on ‘pure’ or go-only blocks (where stop signals are either absent or ignored) to ‘mixed’ blocks of go and stop trials (Boulinguez et al., 2009; Chikazoe et al., 2009; Verbruggen & Logan, 2009; Verbruggen et al., 2014b). It can also be investigated by altering the proportion of incongruent to congruent trials on a Stroop task, thereby manipulating the expectancy of a particular outcome and reducing the amount of response competition (Yücel et al., 2012). Strategic proactive inhibition can also be assessed using modified versions of the go/no-go or stop signal tasks, e.g., (a) altering the probability of stop trials (Verbruggen & Logan, 2009; Zandbelt et al., 2011), (b) varying the number of go trials between stop trials (Vink et al., 2005) or (c) using conditional stop trials that are dependent on a specific response (e.g., only stop when the stop signal appears on the left side of the screen) (e.g., Aron & Verbruggen, 2008; Zandbelt et al., 2011).

While this has not yet been *explicitly* studied in EDs, a number of neuropsychological paradigms, such as those described above, involve manipulations of uncertainty that elicit functions that resemble proactive inhibitory control. For example, post-error slowing demonstrates strategic proactive adjustment of cognitive strategies, trading off speed to improve accuracy in compensation after an error is committed. Wierenga et al. (2014) observed that adolescents with anorexia nervosa (AN) had reduced post-error slowing compared to age-matched healthy controls on the stop signal task in the absence of differences in overall mean reaction time, suggesting that

the patient group had made less proactive adjustment of response strategies. In a study using the Simon Spatial Incompatibility task, while neither healthy adults nor adults with BN demonstrated post-error slowing, participants with BN in fact responded more quickly on post-error trials (Marsh et al., 2009), again suggesting poor strategic use of proactive inhibition.

#### **4. A more simple manifestation of proactive inhibition**

While proactive inhibition can be evidenced through commonly used paradigms (as described above), the tasks are complicated and involve multiple mechanisms, including signal detection, signal identification, attention, determination of signal relevance, action selection, action execution and action monitoring (Verbruggen et al., 2014a). Proactive inhibition on these tasks may also be influenced by working memory, as manipulating the overall context of uncertainty requires an updated representation of the probability that a response is required. Moreover, these tasks are rarely used to *explicitly* study proactive inhibition, rather, they are most often employed in the assessment of other aspects of inhibitory control, such as reactive inhibition or cognitive flexibility (set shifting). Although these different aspects of inhibitory control are typically assessed as independent constructs, they are unlikely to be mutually exclusive systems, e.g., there is evidence that they share overlapping neural substrates that may be differentially employed (for rev, see Aron, 2011; e.g., Zandbelt et al., 2013). Rather, these systems may interact to promote efficient inhibitory control. Thus, the independent role of proactive inhibition in tasks considered to explicitly assess other aspects of inhibition is unclear, as is its contribution to observed deficits in EDs. To begin to address this issue, it is worth exploring a more simple manifestation of proactive inhibition with minimal influence from such confounding factors (see Figure 1 for further illustration). Proactive inhibition can be expressed as a general inhibitory state, in which behavioural responses are withheld in the context of uncertainty (Criaud et al., 2012). This is assessed using paradigms that make use of spatially-uninformative warning cues to indicate an upcoming target compared to non-cued trials, comparing the reaction time of ‘pure’ (cued/non-cued only) blocks compared to mixed blocks of cued and non-cued trials (Boulinguez et al., 2009;



Boulinguez et al., 2008; Criaud et al., 2012; Jaffard et al., 2007; Jaffard et al., 2008). This simple manifestation of proactive inhibition has yet to be studied in EDs.

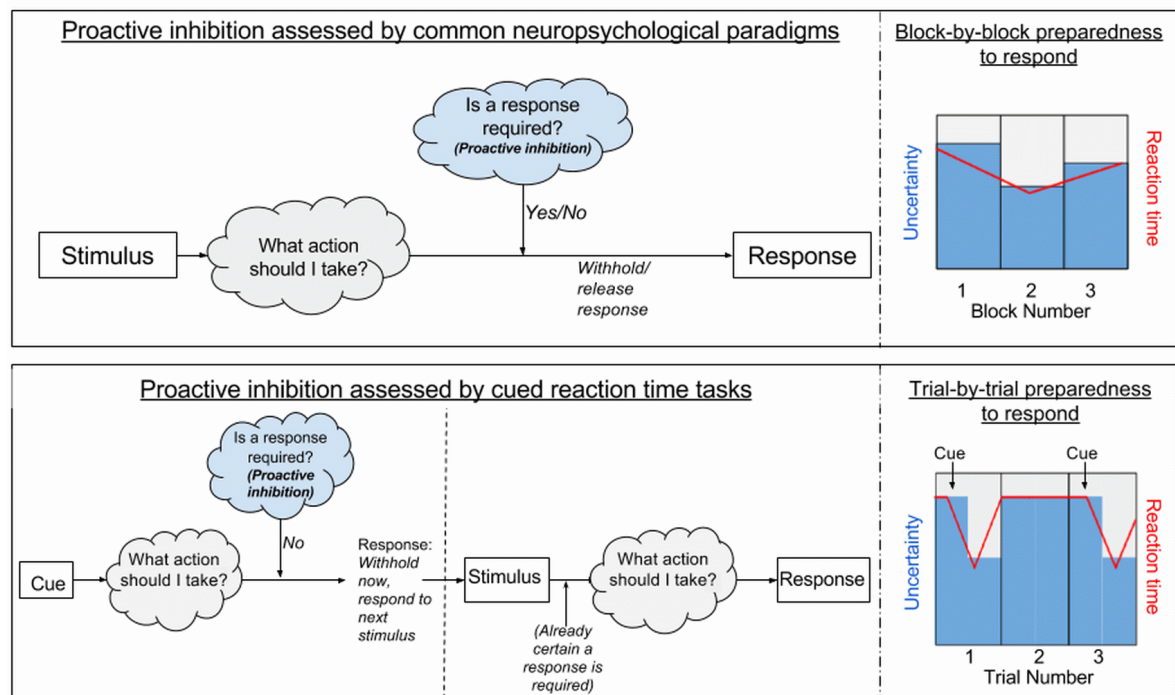


Figure 1. Simplified diagram of how proactive inhibition (blue thought bubble) is manifested in commonly employed neuropsychological tasks of other forms of inhibitory control (e.g., stop signal task), and in simple cued-reaction time tasks. The graphs on the right are intended to provide a hypothetical visual demonstration of how proactive inhibition is reduced as uncertainty regarding the need for a response decreases (blue bars), and the consequent reduction in reaction time (red line). This can be assessed on a trial-by-trial basis using simple cuing paradigms. A global slowing or quickening of reactions can be assessed using any paradigm that can manipulate the overall context of uncertainty (e.g., using a blocked design).

Research on inhibitory control in EDs should be exploring the relative contribution of the different subcomponents of proactive inhibition, reactive inhibition, and reward-based inhibition (e.g., temporal discounting), the different executive mechanisms involved, and their combined contribution to the development and maintenance of inhibitory control- or impulse-related symptoms. Thus, a better understanding of these components and their contribution to behavioural responding, particularly on such neuropsychological or executive tasks, is necessary to determine what is driving any differences in performance. Given the emergence of behavioural interventions for improving inhibitory control using existing neuropsychological paradigms such as the stop signal task or temporal discounting (e.g., for reviews, see Bartholdy et al., 2016; Koffarnus et al., 2013; Turton et al., 2016), this distinction is of particular importance when being used to evaluate what aspects of eating behaviour may benefit most from training in various aspects of inhibitory

control. Thus, it would be worthwhile to explore proactive inhibition in a more simple context to address the questions of (a) whether pure motor proactive inhibition is a component in eating disorders, (b) how it relates to the different ED diagnoses and (c) how it is related to specific ED symptomatology.

## **5. Proactive inhibition and the neural basis of EDs**

Evidence for a potential involvement of simple proactive inhibition in EDs stems from neuroimaging research. Studies assessing proactive inhibition have reported greater activity in the medial prefrontal cortex (mPFC) and inferior parietal cortex (IPC) in non-cued trials (in which proactive inhibition is expected) compared to cued trials (i.e., those preceded by spatially-uninformative cues, in which inhibition is thought to have been released) (Jaffard et al., 2008). Moreover, short cue-delays compared to long cue delays have been associated with greater mPFC and IPC activity and reduced activity in the motor network (primary motor cortex, putamen and supplementary motor area) (Jaffard et al., 2008). These regions have also been implicated in EDs during cognitive tasks and symptom provocation. For example, individuals with EDs exhibit greater mPFC activity and reduced inferior parietal cortex (IPC) activity in response to food stimuli compared to healthy controls (Schienle et al., 2009; Uher et al., 2004; for review in AN, see Zhu et al., 2012). With respect to reactive inhibitory control, studies have revealed that adults recovered from AN showed less activity in the mPFC during hard trials (i.e., those with a long delay between presentation of the go target and the stop cue) of the stop signal task compared to healthy individuals, with no difference on easy trials (i.e., small target-cue delay) (Oberndorfer et al., 2011). Similar findings have been reported in adolescents with AN, who showed reduced recruitment of the middle frontal gyrus bilaterally on hard trials but not easy trials of the stop signal task (Wierenga et al., 2014), and also greater recruitment of the IPC during successful inhibition on the go/no-go task (Lock et al., 2011). AN has also been associated with altered resting functional connectivity between frontal and parietal regions implicated in executive control, with studies reporting increased resting functional connectivity in fronto-parietal networks in adults (Boehm et al., 2014) and reduced resting connectivity in the executive control network

(mPFC, anterior and posterior cingulate cortex; Smith et al., 2009) in adolescents (Gaudio et al., 2015) with AN compared to healthy controls.

Neuroimaging studies in individuals with BED have similarly revealed reduced mPFC and IPL activity during anticipation of reward/losses (Balodis et al., 2013a) and reduced mPFC activity during the Stroop task assessing cognitive inhibition, particularly during incongruent trials where there is a greater requirement for inhibitory control (Balodis et al., 2013b) in individuals with BED compared to non-binge eating obese and normal-weight adults (for review, see Kessler et al., 2016). These regions have also been implicated from studies of BN. For example, recruitment of the right mPFC and IPC during correct responding in a Simon Spatial Incompatibility Task was inversely correlated with frequency of bulimic episodes in adults with BN, suggesting reduced frontostriatal recruitment is associated with greater illness severity (Marsh et al., 2009). Similarly, greater deactivation in these regions were observed in adolescents with BN during correct responding compared to healthy adolescents, and activity in the IPC (precuneus) was negatively associated with symptom severity in BN adolescents (Marsh et al., 2011). Taken together, it is possible that the mPFC and IPC are tonically active and regulate the circuitry that controls basic motor responding. In this way, altered activity in these regions could be related to differences in inhibitory control seen in EDs. Research is required to (a) disentangle the executive ‘inhibition’ and ‘releasing’ mechanisms from attentional (e.g., error monitoring) and sensorimotor processes in order to develop more accurate models of inhibition (Criaud et al., 2012), and (b) better understand how the neural circuitry involved in proactive inhibition relates to inhibitory control, anxiety and symptom experience/expression in EDs.

## **6. Proactive inhibition and anxiety related to uncertainty**

As proactive inhibition occurs in the context of uncertainty, it is likely to be affected by intolerance of uncertainty. This may be particularly relevant in the present context, as intolerance of uncertainty is increased across EDs, especially in AN (Sternheim et al., 2011b). Uncertainty is closely linked to probability and probabilistic reasoning, and therefore uncertainty-related anxiety

may affect behavioural responding where the certainty of a response is varied. Intolerance of uncertainty is associated with a heightened sensitivity to ambiguity, to distress in uncertain situations and to the perception of uncertainty as negative and/or threatening (Buhr & Dugas, 2002). In other words, proactive inhibition will likely be related to the way in which the individual makes decisions in the context of uncertainty: either by delaying responses to reduce the uncertainty (i.e., waiting for more information prior to responding), or by “jumping to conclusions” to reduce the duration in which anxiety is experienced, however a full discussion of such decision making processes is outside the remit of this paper. (For further discussion of potential mechanisms involved in the process of decision making under uncertainty, see Brooks, 2016; and the *Frontiers in Neuroscience* research topic "Decision Making Under Uncertainty", Preuschoff et al., 2013).

Qualitative studies of patients with AN have reported that uncertainty is experienced as stressful, and that where possible, patients wish to minimise the potential for uncertainty (Sternheim et al., 2011a). In addition, patients reported their ED as being more severe in the context of uncertainty, and recognised that they also engaged in eating disordered behaviours as a means of coping with uncertainty (Sternheim et al., 2011a). Individuals with AN and with BN reported greater distress than healthy participants on a decision making task at all levels of certainty/probability (Sternheim et al., 2011b). Moreover, in a study of intolerance of uncertainty (using questionnaires and tasks exploring decision making in the context of ambiguity), individuals with AN attributed greater importance to decision accuracy in their decision making process (Sternheim et al., 2011b). This may also be related to the high levels of perfectionism often reported in AN (Bardone-Cone et al., 2007). Perfectionism and perceived need for control have been hypothesized to influence an individual's need for predictability, and therefore their tolerance/intolerance of uncertainty (Einstein, 2014). Intolerance of uncertainty has been found to fully mediate the relationship between perfectionism and OCD (Reuther et al., 2013), which as described previously is a common comorbid condition in individuals with AN. Indeed, a recent experimental study found that individuals with AN demonstrated elevated perfectionism on two behavioural tasks, indexed

by longer completion times on a text-replication task, and more time checking their work on a bead sorting task (Lloyd et al., 2014). Thus, it is reasonable to propose that individuals with AN will prioritise accuracy over speed of responding, and that intolerance of uncertainty and perfectionism will lead to stronger proactive inhibition (choosing the self-controlled response of withholding action) in AN. If proactive inhibition does contribute to the aetiology of EDs, it is worth investigating whether a reduction in intolerance of uncertainty, or of anxiety more generally, is accompanied by increased efficiency of proactive regulation of behaviour, as changing one's general state of inhibition or 'preparedness to respond' may facilitate other behavioural changes during treatment.

## 7. Conclusion

On the basis of the reviewed literature, we propose that proactive inhibition contributes to the alterations in inhibitory control observed in individuals with an ED. Exploring the role of proactive inhibition in eating disorders will provide important insight into the relationship between anxiety and symptom expression, and would facilitate the development of targeted behavioural interventions that train inhibitory control to improve adaptive eating behaviour. Therefore, future research should explicitly investigate how proactive inhibition (either in its simple or more complicated form) is expressed in EDs, and whether its expression differs across EDs. Behavioural studies should be conducted to assess both forms of proactive inhibition and should use both general (neutral-valenced) and disorder-specific stimuli. In addition, the relation of proactive inhibition at different stages of illness to (a) other forms of inhibitory control (including reactive inhibition, motivational inhibitory control), (b) trait measures (including intolerance of uncertainty, anxiety, novelty seeking) and (c) biological/neurological factors, should be assessed. This will establish if and how these are related and how such factors may interact to influence symptom presentation. Conceptualising proactive inhibitory control in this way is likely to contribute to the understanding of the behavioural phenotypes of EDs.

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## 9. References

- Aron, A.R. 2011. From Reactive to Proactive and Selective Control: Developing a Richer Model for Stopping Inappropriate Responses. *Biol. Psychiatry*. 69, e55-e68.  
<http://dx.doi.org/10.1016/j.biopsych.2010.07.024>
- Aron, A.R., Verbruggen, F. 2008. Stop the presses: Dissociating a selective from a global mechanism for stopping. *Psychol. Sci*. 19, 1146-1153. <http://dx.doi.org/10.1111/j.1467-9280.2008.02216.x>
- Association, A.P., 2013. Diagnostic and Statistical Manual of Mental Disorders. American Psychiatric Publishing, Arlington, VA.
- Balodis, I.M., Kober, H., Worhunsky, P.D., White, M.A., Stevens, M.C., Pearlson, G.D., Sinha, R., Grilo, C.M., Potenza, M.N. 2013a. Monetary Reward Processing in Obese Individuals With and Without Binge Eating Disorder. *Biol. Psychiatry*. 73, 877-886.  
<http://dx.doi.org/10.1016/j.biopsych.2013.01.014>
- Balodis, I.M., Molina, N.D., Kober, H., Worhunsky, P.D., White, M.A., Sinha, R., Grilo, C.M., Potenza, M.N. 2013b. Divergent neural substrates of inhibitory control in binge eating disorder relative to other manifestations of obesity. *Obesity*. 21, 367-377.  
<http://dx.doi.org/10.1002/oby.20068>

- Bardone-Cone, A.M., Wonderlich, S.A., Frost, R.O., Bulik, C.M., Mitchell, J.E., Uppala, S., Simonich, H. 2007. Perfectionism and eating disorders: Current status and future directions. *Clin. Psychol. Rev.* 27, 384-405. <http://dx.doi.org/10.1016/j.cpr.2006.12.005>
- Bartholdy, S., Dalton, B., O'Daly, O.G., Campbell, I.C., Schmidt, U. 2016. A systematic review of the relationship between eating, weight and inhibitory control using the stop signal task. *Neurosci. Biobehav. Rev.* 64, 35-62. <http://dx.doi.org/10.1016/j.neubiorev.2016.02.010>
- Biederman, J., Ball, S.W., Monuteaux, M.C., Surman, C.B., Johnson, J.L., Zeitlin, S. 2007. Are girls with ADHD at risk for eating disorders? Results from a controlled, five-year prospective study. *J. Dev. Behav. Pediatr.* 28, 302-307. <http://dx.doi.org/10.1097/DBP.0b013e3180327917>
- Blinder, B.J., Cumella, E.J., Sanathara, V.A. 2006. Psychiatric Comorbidities of Female Inpatients With Eating Disorders. *Psychosom. Med.* 68, 454-462 <http://dx.doi.org/10.1097/01.psy.0000221254.77675.f5>
- Boulinguez, P., Ballanger, B., Granjon, L., Benraiss, A. 2009. The paradoxical effect of warning on reaction time: demonstrating proactive response inhibition with event-related potentials. *Clin. Neurophysiol.* 120, 730-737. <http://dx.doi.org/10.1016/j.clinph.2009.02.167>
- Boulinguez, P., Jaffard, M., Granjon, L., Benraiss, A. 2008. Warning signals induce automatic EMG activations and proactive volitional inhibition: evidence from analysis of error distribution in simple RT. *J. Neurophysiol.* 99, 1572-1578. <http://dx.doi.org/10.1152/jn.01198.2007>
- Brooks, S.J. 2016. A debate on working memory and cognitive control: can we learn about the treatment of substance use disorders from the neural correlates of anorexia nervosa? *BMC Psychiatry.* 16, 1. <http://dx.doi.org/10.1186/s12888-016-0714-z>
- Brooks, S.J., Rask-Andersen, M., Benedict, C., Schiöth, H.B. 2012. A debate on current eating disorder diagnoses in light of neurobiological findings: is it time for a spectrum model? *BMC Psychiatry.* 12, 76. <http://dx.doi.org/10.1186/1471-244X-12-76>

- Buhr, K., Dugas, M.J. 2002. The intolerance of uncertainty scale: Psychometric properties of the English version. *Behav. Res. Ther.* 40, 931-945. [http://dx.doi.org/10.1016/S0005-7967\(01\)00092-4](http://dx.doi.org/10.1016/S0005-7967(01)00092-4)
- Calero - Elvira, A., Krug, I., Davis, K., López, C., Fernández - Aranda, F., Treasure, J. 2009. Meta - analysis on drugs in people with eating disorders. *Eur. Eat. Disord. Rev.* 17, 243-259. <http://dx.doi.org/10.1002/erv.936>
- Chikazoe, J., Jimura, K., Hirose, S., Yamashita, K.-i., Miyashita, Y., Konishi, S. 2009. Preparation to inhibit a response complements response inhibition during performance of a stop-signal task. *J. Neurosci.* 29, 15870-15877. <http://dx.doi.org/10.1523/JNEUROSCI.3645-09.2009>
- Criaud, M., Wardak, C., Ben Hamed, S., Ballanger, B., Boulinguez, P. 2012. Proactive inhibitory control of response as the default state of executive control. *Front. Psychol.* 3, 59. <http://dx.doi.org/10.3389/fpsyg.2012.00059>
- Davis, C., Patte, K., Curtis, C., Reid, C. 2010. Immediate pleasures and future consequences. A neuropsychological study of binge eating and obesity. *Appetite.* 54, 208-213. <http://dx.doi.org/10.1016/j.appet.2009.11.002>
- Einstein, D.A. 2014. Extension of the transdiagnostic model to focus on intolerance of uncertainty: a review of the literature and implications for treatment. *Clinical Psychology: Science and Practice.* 21, 280-300. <http://dx.doi.org/10.1111/cpsp.12077>
- Fernández-Aranda, F., Pinheiro, A.P., Thornton, L.M., Berrettini, W.H., Crow, S., Fichter, M.M., Halmi, K.A., Kaplan, A.S., Keel, P., Mitchell, J., Rotondo, A., Strober, M., Woodside, D.B., Kaye, W.H., Bulik, C.M. 2008. Impulse control disorders in women with eating disorders. *Psychiatry Res.* 157, 147-157. <http://dx.doi.org/10.1016/j.psychres.2007.02.011>
- Franko, D.L., Keel, P.K. 2006. Suicidality in eating disorders: occurrence, correlates, and clinical implications. *Clin. Psychol. Rev.* 26, 769-782. <http://dx.doi.org/10.1016/j.cpr.2006.04.001>
- Gadalla, T., Piran, N. 2007. Co-occurrence of eating disorders and alcohol use disorders in women: a meta analysis. *Archives of Women's Mental Health.* 10, 133-140. <http://dx.doi.org/10.1007/s00737-007-0184-x>



- Galimberti, E., Martoni, R.M., Cavallini, M.C., Erzegovesi, S., Bellodi, L. 2012. Motor inhibition and cognitive flexibility in eating disorder subtypes. *Prog. Neuropsychopharmacol. Biol. Psychiatry.* 36, 307-312. <http://dx.doi.org/10.1016/j.pnpbp.2011.10.017>
- Golden, N.H., Katzman, D.K., Sawyer, S.M., Ornstein, R.M., Rome, E.S., Garber, A.K., Kohn, M., Kreipe, R.E. 2015. Update on the Medical Management of Eating Disorders in Adolescents. *J. Adolesc. Health.* 56, 370-375.  
<http://dx.doi.org/10.1016/j.jadohealth.2014.11.020>
- Hudson, J.I., Hiripi, E., Pope Jr, H.G., Kessler, R.C. 2007. The Prevalence and Correlates of Eating Disorders in the National Comorbidity Survey Replication. *Biol. Psychiatry.* 61, 348-358. <http://dx.doi.org/10.1016/j.biopsych.2006.03.040>
- Jaffard, M., Benraiss, A., Longcamp, M., Velay, J.-L., Boulinguez, P. 2007. Cueing method biases in visual detection studies. *Brain Res.* 1179, 106-118.  
<http://dx.doi.org/10.1016/j.brainres.2007.08.032>
- Jaffard, M., Longcamp, M., Velay, J.-L., Anton, J.-L., Roth, M., Nazarian, B., Boulinguez, P. 2008. Proactive inhibitory control of movement assessed by event-related fMRI. *NeuroImage.* 42, 1196-1206. <http://dx.doi.org/10.1016/j.neuroimage.2008.05.041>
- Kaye, W.H., Bulik, C.M., Thornton, L., Barbarich, N., Masters, K. 2004. Comorbidity of anxiety disorders with anorexia and bulimia nervosa. *Am. J. Psychiatry.* 161, 2215-2221.  
<http://dx.doi.org/10.1176/appi.ajp.161.12.2215>
- Kaye, W.H., Wierenga, C.E., Bailer, U.F., Simmons, A.N., Wagner, A., Bischoff-Grethe, A. 2013. Does a Shared Neurobiology for Foods and Drugs of Abuse Contribute to Extremes of Food Ingestion in Anorexia and Bulimia Nervosa? *Biol. Psychiatry.* 73, 836-842.  
<http://dx.doi.org/10.1016/j.biopsych.2013.01.002>
- Kaye, W.H., Wierenga, C.E., Knatz, S., Liang, J., Boutelle, K., Hill, L., Eisler, I. 2015. Temperament - based Treatment for Anorexia Nervosa. *Eur. Eat. Disord. Rev.* 23, 12-18.  
<http://dx.doi.org/10.1002/erv.2330>

- Kekic, M., Bartholdy, S., Cheng, J., McClelland, J., Boysen, E., Musiat, P., O'Daly, O.G., Campbell, I.C., Schmidt, U. 2016. Increased temporal discounting in bulimia nervosa. *Int. J. Eat. Disord.*, Epub ahead of print. <http://dx.doi.org/10.1002/eat.22571>
- Kessler, R.M., Hutson, P.H., Herman, B.K., Potenza, M.N. 2016. The neurobiological basis of binge-eating disorder. *Neurosci. Biobehav. Rev.* 63, 223-238. <http://dx.doi.org/10.1016/j.neubiorev.2016.01.013>
- Koffarnus, M.N., Jarmolowicz, D.P., Mueller, E.T., Bickel, W.K. 2013. Changing delay discounting in the light of the competing neurobehavioral decision systems theory: a review. *J. Exp. Anal. Behav.* 99, 32-57. <http://dx.doi.org/10.1002/jeab.2>
- Lipszyc, J., Schachar, R. 2010. Inhibitory control and psychopathology: a meta-analysis of studies using the stop signal task. *J. Int. Neuropsychol. Soc.* 16, 1064-1076. <http://dx.doi.org/10.1017/S1355617710000895>
- Lloyd, S., Yiend, J., Schmidt, U., Tchanturia, K. 2014. Perfectionism in Anorexia Nervosa: Novel Performance Based Evidence. *PLoS One.* 9, e111697. 10.1371/journal.pone.0111697
- Lock, J., Garrett, A., Beenhakker, J., Reiss, A.L. 2011. Aberrant brain activation during a response inhibition task in adolescent eating disorder subtypes. *Am. J. Psychiatry.* <http://dx.doi.org/10.1176/appi.ajp.2010.10010056>
- Manwaring, J.L., Green, L., Myerson, J., Strube, M.J., Wilfley, D.E. 2011. Discounting of various types of rewards by women with and without binge eating disorder: Evidence for general rather than specific differences. *Psychol. Rec.* 61, 4.
- Marsh, R., Horga, G., Wang, Z., Wang, P., Klahr, K.W., Berner, L.A., Walsh, B.T., Peterson, B.S. 2011. An FMRI study of self-regulatory control and conflict resolution in adolescents with bulimia nervosa. *Am. J. Psychiatry.* <http://dx.doi.org/10.1176/appi.ajp.2011.11010094>
- Marsh, R., Steinglass, J.E., Gerber, A.J., Graziano O'Leary, K., Wang, Z., Murphy, D., Walsh, B.T., Peterson, B.S. 2009. Deficient activity in the neural systems that mediate self-regulatory control in bulimia nervosa. *Arch. Gen. Psychiatry.* 66, 51. <http://dx.doi.org/10.1001/archgenpsychiatry.2008.504>

- Mole, T., Irvine, M., Worbe, Y., Collins, P., Mitchell, S., Bolton, S., Harrison, N., Robbins, T., Voon, V. 2015. Impulsivity in disorders of food and drug misuse. *Psychol. Med.* 45, 771-782. <http://dx.doi.org/10.1017/S0033291714001834>
- Nazar, B.P., Pinna, C.M.d.S., Coutinho, G., Segenreich, D., Duchesne, M., Appolinario, J.C., Mattos, P. 2008. Review of literature of attention-deficit/hyperactivity disorder with comorbid eating disorders. *Rev. Bras. Psiquiatr.* 30, 384-389. <http://dx.doi.org/10.1590/S1516-44462008000400014>
- Oberndorfer, T.A., Kaye, W.H., Simmons, A.N., Strigo, I.A., Matthews, S.C. 2011. Demand-specific alteration of medial prefrontal cortex response during an inhibition task in recovered anorexic women. *Int. J. Eat. Disord.* 44, 1-8. <http://dx.doi.org/10.1002/eat.20750>
- Preuschoff, K., Mohr, P.N., Hsu, M. 2013. Decision making under uncertainty. *Front. Neurosci.* 7. <http://dx.doi.org/10.3389/fnins.2013.00218>
- Reuther, E.T., Davis, T.E., Rudy, B.M., Jenkins, W.S., Whiting, S.E., May, A.C. 2013. Intolerance of uncertainty as a mediator of the relationship between perfectionism and obsessive - compulsive symptom severity. *Depress. Anxiety.* 30, 773-777. <http://dx.doi.org/10.1002/da.22100>
- Schienle, A., Schäfer, A., Hermann, A., Vaitl, D. 2009. Binge-eating disorder: reward sensitivity and brain activation to images of food. *Biol. Psychiatry.* 65, 654-661. <http://dx.doi.org/10.1016/j.biopsych.2008.09.028>
- Steinglass, J.E., Figner, B., Berkowitz, S., Simpson, H.B., Weber, E.U., Walsh, B.T. 2012. Increased capacity to delay reward in anorexia nervosa. *J. Int. Neuropsychol. Soc.* 18, 773-780. <http://dx.doi.org/10.1017/S1355617712000446>
- Sternheim, L., Konstantellou, A., Startup, H., Schmidt, U. 2011a. What does uncertainty mean to women with anorexia nervosa? An interpretative phenomenological analysis. *Eur. Eat. Disord. Rev.* 19, 12-24. <http://dx.doi.org/10.1002/erv.1029>
- Sternheim, L., Startup, H., Schmidt, U. 2011b. An experimental exploration of behavioral and cognitive-emotional aspects of intolerance of uncertainty in eating disorder patients. *J. Anxiety Disord.* 25, 806-812. <http://dx.doi.org/10.1016/j.janxdis.2011.03.020>

- Svaldi, J., Naumann, E., Trentowska, M., Schmitz, F. 2014. General and food-specific inhibitory deficits in binge eating disorder. *The International journal of eating disorders*.  
<http://dx.doi.org/10.1371/10.1002/eat.22260>
- Turton, R., Bruidegom, K., Cardi, V., Hirsch, C.R., Treasure, J. 2016. Novel methods to help develop healthier eating habits for eating and weight disorders: A systematic review and meta-analysis. *Neurosci. Biobehav. Rev.* 61, 132-155.  
<http://dx.doi.org/10.1016/j.neubiorev.2015.12.008>
- Uher, R., Murphy, T., Brammer, M.J., Dalgleish, T., Phillips, M.L., Ng, V.W., Andrew, C.M., Williams, S.C., Campbell, I.C., Treasure, J. 2004. Medial prefrontal cortex activity associated with symptom provocation in eating disorders. *Am. J. Psychiatry.* 161, 1238-1246. <http://dx.doi.org/10.1176/appi.ajp.161.7.1238>
- Verbruggen, F., Logan, G.D. 2009. Proactive adjustments of response strategies in the stop-signal paradigm. *J. Exp. Psychol. Hum. Percept. Perform.* 35, 835.  
<http://dx.doi.org/10.1037/a0012726>
- Verbruggen, F., McLaren, I.P., Chambers, C.D. 2014a. Banishing the control homunculi in studies of action control and behavior change. *Perspect. Psychol. Sci.* 9, 497-524.  
<http://dx.doi.org/10.1177/1745691614526414>
- Verbruggen, F., Stevens, T., Chambers, C.D. 2014b. Proactive and reactive stopping when distracted: An attentional account. *J. Exp. Psychol. Hum. Percept. Perform.* 40, 1295.  
<http://dx.doi.org/10.1037/a0036542>
- Vink, M., Kahn, R.S., Raemaekers, M., van den Heuvel, M., Boersma, M., Ramsey, N.F. 2005. Function of striatum beyond inhibition and execution of motor responses. *Hum. Brain Mapp.* 25, 336-344. <http://dx.doi.org/10.1002/hbm.20111>
- Wierenga, C., Bischoff-Grethe, A., Melrose, A.J., Grenesko-Stevens, E., Irvine, Z., Wagner, A., Simmons, A., Matthews, S., Yau, W.Y., Fennema-Notestine, C., Kaye, W.H. 2014. Altered BOLD response during inhibitory and error processing in adolescents with anorexia nervosa. *PLoS One.* 9, e92017. <http://dx.doi.org/10.1371/journal.pone.0092017>

- Wu, M., Giel, K.E., Skunde, M., Schag, K., Rudofsky, G., de Zwaan, M., Zipfel, S., Herzog, W., Friederich, H.-C. 2013a. Inhibitory control and decision making under risk in bulimia nervosa and binge-eating disorder. *Int. J. Eat. Disord.* 46, 721-728.  
<http://dx.doi.org/10.1002/eat.22143>
- Wu, M., Hartmann, M., Skunde, M., Herzog, W., Friederich, H.C. 2013b. Inhibitory control in bulimic-type eating disorders: A systematic review and meta-analysis. *PLoS One.* 8, e83412. <http://dx.doi.org/10.1371/journal.pone.0083412>
- Yücel, M., Fornito, A., Youssef, G., Dwyer, D., Whittle, S., Wood, S.J., Lubman, D.I., Simmons, J., Pantelis, C., Allen, N.B. 2012. Inhibitory control in young adolescents: The role of sex, intelligence, and temperament. *Neuropsychology.* 26, 347.  
<http://dx.doi.org/10.1371/10.1037/a0027693>
- Zandbelt, B.B., Bloemendaal, M., Neggers, S.F., Kahn, R.S., Vink, M. 2013. Expectations and violations: delineating the neural network of proactive inhibitory control. *Hum. Brain Mapp.* 34, 2015-2024. <http://dx.doi.org/10.1002/hbm.22047>
- Zandbelt, B.B., van Buuren, M., Kahn, R.S., Vink, M. 2011. Reduced proactive inhibition in schizophrenia is related to corticostriatal dysfunction and poor working memory. *Biol. Psychiatry.* 70, 1151-1158. <http://dx.doi.org/10.1016/j.biopsych.2011.07.028>
- Zandbelt, B.B., Vink, M. 2010. On the Role of the Striatum in Response Inhibition. *PLoS One.* 5, e13848. <http://dx.doi.org/10.1371/journal.pone.0013848>
- Zhu, Y., Hu, X., Wang, J., Chen, J., Guo, Q., Li, C., Enck, P. 2012. Processing of Food, Body and Emotional Stimuli in Anorexia Nervosa: A Systematic Review and Meta - analysis of Functional Magnetic Resonance Imaging Studies. *Eur. Eat. Disord. Rev.* 20, 439-450.  
<http://dx.doi.org/10.1002/erv.2197>